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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,808	03/15/2000	Athanasius A Anagnostou	5218-39C	9764

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/525,808	ANAGNOSTOU ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed after final on 7/25/2002 (paper no. 11) is acknowledged and entered into the record. Accordingly, claims 23-29 are canceled without prejudice.

2. Therefore, claims 16-22 are pending and examined on the record.

3. The Finality of the instant application is withdrawn in light of new claim rejections.Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 7/25/2002 has been entered.

4. Currently, claims 23-29 were rejected under 35 USC 112, 1st paragraph as lacking written description, however, the rejection is withdrawn in light of the cancellation of the claims.

Information Disclosure Statement

5. The Information Disclosure Statement filed 7/16/2002 (paper no. 10) is acknowledged and considered. A signed copy of the IDS is attached hereto.

New Claim Rejections- 35 USC § 112, 2nd paragraph

6. Claims 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claim 16 and dependent claims thereof, in the recitation of "mechanical damage", it is unclear as to the metes and bounds of the term, because the

definition has not been provided in the specification. It is not clear as to whether mechanical damage is intended to encompass damage caused by chemical exposure.

8. Regarding claim 16 and dependent claims thereof, the metes and bounds of the term "amount" cannot be determined because the intended "amount" is not defined in the specification.

9. Claims 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps involve when and how to determine treatment of endothelial cell injury.

New Claim Rejections- 35 USC § 112, 1st paragraph

10. Claims 16-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method of protecting endothelial cells from the chemotherapeutic damage of cisplatin, comprising the administration of erythropoietin (EPO), does not reasonably provide enablement for a method of treating endothelial cell injury, caused by mechanical damage, exposure to radiation, inflammation, heart disease, cancer, or other chemotherapeutics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the

same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a method of treating endothelial injury caused by mechanical damage, exposure to radiation, inflammation, heart disease or cancer comprising the administration of an endothelial protecting amount of EPO to a subject.

The amount of direction or guidance present and the presence or absence of working examples: The examples of the instant invention are drawn to the endothelial protecting effects of EPO, at specific dose ranges and in an in vitro culture system, on the exposure of endothelial cells before, concurrently, and after to cisplatin. The protective

effects are measure by the percent viability of the cells following endothelial cell exposure to cisplatin alone, or in combination with EPO in vitro. However, nowhere in the specification does it teach the protective effects of EPO on any other type of chemotherapeutics. Perhaps, the effects of EPO on cisplatin are chemotherapeutic specific, because the EPO counteracts the specific toxic effect cisplatin has on cells. Further, the instant specification has not taught how the administration of EPO to cells that are damaged from heart disease, inflammation, or mechanical damage is to respond to the administration of EPO and or whether such administration would be enabling within the scope of the claims. Further still, the specification alludes to the fact that the protective effects of EPO are dose dependent, wherein there exists a biphasic effect of EPO on endothelial cell proliferation. Such biphasic effects include endothelial cell proliferation at lower dosages and endothelial cell inhibition of growth at higher dosages. The instant specification has only taught a dose range of 0.15-5 U/ml (on the lower range of dosages) of EPO as an endothelial protecting amount *in vitro*. Such an amount would be within the scope of the claims, wherein any variation from this dose may cause one of skill in the art to experiment to determine if the dose administered to the cell would be effective or deleterious to cell proliferation. And lastly, the specification has not taught to one of skill in the art how to protect endothelial cell from damage in vivo. There is no guidance as to how the EPO is to be administered, the actual dosage needed to protect cells from damage, whether the EPO when administered to cells in vivo will have a biphasic effect, and whether it does indeed protect cells from damage. As such the specification has limited the instant invention to

a method of protecting endothelial cells from cisplatin damage in vitro comprising the administration of EPO within the ranges 0.15-5U/ml, wherein the protective effect is interpreted as continued proliferation of endothelial cells in culture.

The breadth of the claims and the quantity of experimentation needed: Given the lack of guidance in the specification as to teach one of skill in the art how to protect cells from mechanical damage, radiation damage, inflammation, heart disease, or cancer, and the effects of EPO in vivo, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 16 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Carlini *et al* (Kidney Int. 1995 Mar.;47(3):740-5, IDS). Claim 16 and 21 are drawn to a method of treating endothelial injury comprising the administration of EPO, wherein the injury is caused by cancer. It is noted that endothelial cell protection is interpreted to read on cells that retain the ability to proliferate. Calini *et al* teach that EPO is able to stimulate endothelial cell proliferation in the form of endothelial cell stimulated angiogenesis. Angiogenesis, is the growth of endothelial cell blood vessels from pre-existing blood vessels and can be stimulated by cancer. Furthermore, Calini *et al* teach

that such administration can be inhibited if EPO antibodies are present with EPO, thereby demonstrating the role of EPO on endothelial cell proliferation.

Conclusion

No claim is allowed. This rejection is made **NON-FINAL** in view of the newly cited claim rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
January 16, 2003

ALI R. SALIMI
PRIMARY EXAMINER